Allergy Abstracts

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Asthma and Hay Fever

Bronchomotor Tone: A Neglected Factor in the Regulation of the Pulmonary Circulation. Rodbard, S.: Am. J. Med. **15**: 356, 1953.

According to one theory pulmonary circulation is controlled by vasomotor regulation of the pulmonary arterial pressure and blood flow. A second theory diametrically opposed regards pulmonary circulation as a purely passive affair with the blood flowing downhill from the right ventricle to the lower pressure level of the left auricle. Many facts are cited both in support of and in contradiction to each concept.

The author advances the theory that it is bronchomotor tone which is the principal factor in regulating pulmonary circulation. Changes in the intra-alveolar pressure resulting from constriction and dilatation of the bronchi and bronchioles in expiration and inspiration have a direct effect upon the size of the arterioles and capillaries of the lung bed and thus affect the pulmonary circulation. Drugs such as acetylcholine and histamine, which are known to cause a transient rise in the pulmonary diastolic pressure, do so through the increased bronchomuscular tone which they induce. Also, morphine, which is a well-known bronchoconstrictor, produces a heightened alveolar pressure which may account for its effectiveness in the treatment of pul-

monary edema. This bronchoconstrictor effect of morphine may, however, be the cause for its deleterious and sometimes fatal action in such conditions as bronchial asthma and other chronic pulmonary and cardiopulmonary diseases. F.

A Study of the Hay Fever-Causing Pollen in the Paris Region. Tabort, J., and Bimont, G.: Presse méd. **61**: 545, 1953.

Clinical studies of hay fever and weekly botanical surveys of plants and pollination were made in the Paris region from March to October of 1951 and 1952. Pollen counts were not done. The most common plants encountered were grasses, represented by 340 species, not including the cereals which are cultivated in large quantities. The most common offenders among the grasses and their pollination periods are tabulated. As a rule, pollination started at the end of the spring and terminated in the middle of the summer. Tree pollens were responsible in most cases for hay fever from February to June. A detailed list of trees and their pollination periods is given. Of the weeds the most common offenders were Rumex-like curled dock and sheep sorrel, the plantains and the cypresses. Of the Compositae family, pollinating from July to September, the most common offenders were the Artemesias. The Chenopods caused late hay fever. Intracutaneous tests with extracts of the most common pollens were performed on 101 hay fever patients. Eighty-nine per cent were found to be sensitive to grasses, 55 per cent were sensitive to trees, and 65 per cent were sensitive to some weeds. I. Glazer.

Dramatic Relief of Hay Fever Symptoms With Combined Amphetamine and Amobarbital. Woodrow, M.: Am. Pract.—Digest Treat. **4**: 441, 1953.

Dexamyl, a combination of d-amphetamine and amobarbital, was found to be effective in the symptomatic relief of hay fever. Among a total of 22 patients who were treated with one tablet of the drug three times daily, 12 obtained excellent relief, 9 good relief, and 1 no relief. In only 1 patient was nervousness a troublesome side effect. F.

Dermatology

Studies of Skin-Hypersensitivity to Lanolin. Sulzberger, M. B., Warshaw, T., and Herrmann, F.: J. Invest. Dermat. **20**: 33, 1953.

Of 1,048 dermatologic patients patch tested with anhydrous lanolin (U.S.P.), 12 showed positive reactions. One hundred twenty healthy volunteers similarly tested showed completely negative reactions. The positive responses varied in intensity from mild erythema to infiltration with extensive blister formation. Eighteen subjects known to be contact-sensitive to lanolin were given inunctions with 3 different samples of lanolin (2 anhydrous, one hydrous). Positive responses were obtained in 2 cases with all 3 samples of lanolin.

All the positive reactors were patch tested with several brands of lanolin (U.S.P.) as well as with lanolin derivatives and several of the constituent fractions. The acetylated derivative of lanolin produced positive reactions in 6 of 12 patients, whereas the propionylated form of lanolin caused only 3 positive reactions in the 12 patients. Cholesterol consistently gave negative reactions. The fractions defined as the "lanolin-alcohols" and the "aliphatic alcohol fraction" possessed the strongest allergenic activity. Eleven of 12 patients hypersensitive to lanolin showed a positive patch reaction to the unmodified aliphatic alcohol fraction, but only one of these subjects reacted

to this same compound following its acetylation. It is suggested that one or more of the aliphatic alcohols of lanolin are responsible for the hypersensitivity reactions to lanolin. R. W.

Cortisone in the Treatment of Acute Self-Limited Dermatoses. Wrong, N. M., and Smith, R. C.: Canad. M. A. J. **68**: 50, 1953.

Thirty-two hospitalized patients with various allergic dermatoses were treated with oral cortisone. Twenty-two patients had contact dermatitis, 6 urticaria, and 4 had various other types of reactions. Most of the cases of dermatitis were caused by *Rhus radicans,* but a few were produced by miscellaneous chemicals. Penicillin was the incitant that stimulated most of the urticarial reactions. The average dose of cortisone ranged from 500 to 1,000 mg. About one-half the patients had excellent results and another 25 per cent had good results, while the remaining cases obtained no relief. One patient with seborrhea and contact dermatitis expired following a massive gastric hemorrhage. The average length of hospitalization was almost cut in half with this therapy. The authors suggest continuing the drug for several days after cessation of the reaction in order to prevent a recurrence of the pruritus. They warn against the indiscriminate use of cortisone in cases where the etiology is undetermined. R. W.

Some Endocrine Aspects of Skin Sensitization and Primary Irritation. III. Observations on the Influence of Cold Exposure and Formalin Treatment (Systemic Stress) Upon Cutaneous Irritation and Sensitization. Nilzen, Ake: J. Invest. Dermat. **20**: 185, 1953.

Guinea pigs sensitized to 30 per cent 2,4-dinitrochlorobenzene (DNB) were exposed to various stress stimuli. One group of animals was kept at 4° C. for six or seven hours while the other group was injected subcutaneously with 1 ml. of 10 per cent formalin solution. Croton oil was used as a primary irritant in order to study the effect of stress reactions upon nonspecific excitants. While the animals were under the influence of the stress stimuli, the skin responses to DNB were milder and the interval between exposure to the antigen and appearance of the response was delayed. Skin reactivity increased considerably forty-eight hours following stress stimuli, but ten days later approximated normal levels. The adrenals were definitely enlarged and heavier following the stress reactions. Croton oil produced less edema and erythema following the stress reaction with a delay in the onset of the necrotic response. Forty-eight hours later, however, just as with specific excitants, there was increased skin reactivity. It is suggested that the stress reactions produced corticoadrenal stimulation which was responsible for altering the skin responses. R. W.

Super-Ego and Aggression in Circumscribed Neurodermatitis. Seitz, P. F. D., Gosman, J. S., and Craton, J.: J. Invest. Dermat. **20**: 263, 1953.

Thirty-five patients with localized neurodermatitis, who were willing and had the intelligence to understand a psychological test, were studied. The control group consisted of 29 individuals with pruritus presumably due to nonpsychogenic skin disorders. Patients in each category were selected from the same source and approximated each other in age, sex, rate, and duration and severity of dermatologic disease. "The Rosenzweig Picture-Frustration Test was used to determine quantitatively the degree of punitiveness of the Superego and the degree of masochistic expression of aggressiveness." The

patient was asked in the test to interpret what he saw in 24 standard cartoon-like picture situations. The placards depicted an individual experiencing various kinds of everyday frustration at the hands of other people. All testing was done by the same individual. Responses were graded without knowledge of the dermatologic disorder and the results classified according to the direction of aggression as extrapunitive, intropunitive, and impunitive. Extrapunitive indicated overtly expressed aggressiveness, intropunitive indicated expressed aggressiveness against oneself, and impunitive implied no expressed aggressiveness in any particular direction. It was found that neurodermatitic patients gave a higher number of intropunitive responses than were obtained from controls and that these patients tended to express aggressiveness masochistically. R. W.

Eosinophile in Human Skin Homografting. Rogers, B. O., Converse, J. M., Taylor, A. C., and Campbell, R. M.: Proc. Soc. Exper. Biol. & Med. **82**: 523, 1953.

The circulating and tissue eosinophiles were studied in 10 human cases of full-thickness skin homografting. The eosinophiles in the tissues were determined by counting 400 oil immersion fields in biopsy specimens taken from the edge of the graft. Several cases of autograftings served as controls. The circulating eosinophile counts were more than twice the normal in 6 of the 10 homograftings; in none of the autograftings did the count exceed twice the normal range. The tissue eosinophilia was found comparable in magnitude to the intensity of the circulatory eosinophilia. The highest eosinophilia occurred when the epithelium of the homograft had sloughed and only intact dermis remained. As the dermal pad sloughed away, the counts gradually returned to normal levels. The increase in eosinophiles was accompanied by a proportionate fall in polymorphonuclear cells. M. Cohen.

Dermatitis From Water Glass. Caused by Synergistic Action With an Alkaline Detergent. Morris, G. E.: Arch. Ind. Hyg. & Occ. Med. **7**: 411, 1953.

Dermatitis from water glass (sodium silicate) has been previously reported on several occasions. The author describes 2 cases of dermatitis which occurred when an alkaline detergent was used after handling water glass. Patch reactions to water glass were negative in one case and positive in the other, but both patients gave positive patch reactions to a mixture of the water glass and the alkaline detergent. A mixture of the water glass and acid-reacting detergent yielded negative patch reactions in both cases. The patients were able to continue working with water glass when the acid detergent was substituted for the alkaline one. F.

Experimental Histamine Pruritus. II. Nature; Physical and Environmental Factors Influencing Development and Severity. Cormia, E. F., and Kuykendall, V.: J. Invest. Dermat. **20**: 429, 1953.

An itch threshold in human subjects was obtained by determining the weakest dilution of histamine which produced pruritus upon intracutaneous injection. This threshold varied between a 1:1000 and 1:10,000,000 dilution of histamine phosphate solution, with most patients in the 1:100,000 range. Approximately 10 per cent of the subjects, usually those over 50 years of age, failed to have an itch response. The itch threshold varied considerably in different parts of the body, although corresponding areas on opposite forearms appeared to respond uniformly. The threshold tended to fall at night and when skin temperature was elevated. No significant alterations in threshold developed during the various phases of the menstrual cycle.

The flare reaction and not the wheal was closely correlated with histamine-induced itching. When whealing was suppressed by application of a pressure cuff above the injection site, the flare remained unchanged and normal itching developed.

Repeated injections of histamine into a site produced a loss of response. Some sensitivity returned in a few subjects after 1 hour. In 1 subject, mild pruritus developed on retesting such a site at 24 hours, and the full sensation of pruritus returned at 48 hours. It was suggested that severe excoriations produced by scratching may liberate excessive histamine with resultant temporary refractoriness of the tissue, thus explaining the intermittent nature of itching in many dermatoses. M. Cohen.

Zirconium-Pyribenzamine Cream for the Prophylaxis of Rhus Dermatitis. Strauss, R. E., and Bruck, C.R.: J. Invest. Dermat. **20**: 411, 1953.

Zirconium, an element, has been found to inactivate urushiol in vitro and to prevent the development of Rhus dermatitis in human beings when applied soon after Rhus toxin has come in contact with the skin. A cream containing 4 per cent zirconium hydrate and 2 per cent Pyribenzamine hydrochloride in a water-soluble base was tested as a prophylactic agent against poison oak among soldiers. The soldiers applied the cream on the exposed areas of the body immediately upon arrival at a bivouac area which was covered with *Rhus diversiloba*. Reapplications were made on arising each morning and during the day after washing. Poison oak dermatitis developed in approximately 10 per cent of the subjects who had used the cream and in approximately 20 per cent of the controls. It could not be determined from this study whether the beneficial results were due to the zirconium, the Pyribenzamine, or to a combination of the two agents. M. Cohen.

Studies of a Nitrocellulose Silicone Cream as a Skin Protectant Against Eczematogenous Contact Allergens. Smith, C. C., Day, T. L., and Zimmerman, E. H.: J. Invest. Dermat. **21**: 111, 1953.

Graded dilutions of Rhus, nickel sulfate, and benzocaine were used to test 36 subjects with known eczematous contact sensitivities to one or more of these allergens. The open skin test method was used in an attempt to reproduce actual clinical conditions of contact. One series of tests was applied to sites previously prepared by inunctions of Covicone, a special plasticized combination of silicone, nitrocellulose, and castor oil suspended in a greaseless, colorless vanishing cream base. Protection in varying degree was present on the inuncted sites in 30 of the 36 subjects. In one case the skin test response was greater on the prepared site than on the control site. The protective effect of the silicone cream tended to increase with the number of days of its application prior to testing. Covicone was effective even when the sites of application were washed prior to testing. No allergic sensitivities to Covicone were encountered. A pustular eruption which developed at the sites of application in two subjects was attributed to occlusion of the sweat or sebaceous ducts. M. Cohen.

Clinical Trials of the Treatment of Eczema and Pruritus by Topical Application of Hydrocortisone Acetate. Sidi, E., Bourgeois-Cavardin, J., and Plas, G.: Presse méd. **61**: 922, 1953.

Forty-one patients with long-standing resistant dermatoses were treated by inunction of minute quantities of hydrocortisone acetate (compound F) ointment from one to three times weekly. There was an immediate and striking disappearance of pruritus even in the most severe cases. The effect usually

lasted as long as 12 hours following the first application. With subsequent applications, the response lasted even longer. When the treatment was discontinued before the disease was cured, the pruritus recurred and became worse. The 2.5 per cent ointment was much more effective than the 1 per cent ointment. The ointment was well tolerated on oozing edematous lesions and dried up even the most acute dermatitis. In erythematous and erythematosquamous lesions, there was a reduction of erythema followed by marked desquamation. About six applications within a period of 10 days were usually adequate to cure a chronic and localized dermatitis-like eczema of the eyelids and anal or vulvar pruritus. In some cases, the treatment had to be continued for weeks since an interruption caused relapses. The ointment base and excipient were much less effective than compound F. When applied to one side of a symmetrical lesion, some beneficial effects were noted on distant lesions to which the ointment had not been directly applied. In some cases of chronic eczema of the eyelids, nummular eczema, and contact dermatitis, the improvement lasted for several weeks. In diathetic (atopic) and seborrheic eczemas, relapses occurred within several days. The ointment was nonirritating and caused no sensitization in the short period of study.

I. Glazer.

Otorhinology and Ophthalmology

Investigation of the Effects of Some New Vasoconstrictors and a New Antiseptic on the Nasal Mucous Membranes of Rabbits. Richtner, N.: Acta oto-larying. **93**: 1951.

A series of experiments were performed on rabbits to determine the effects of certain new vasoconstrictors on the ciliary activity of the nasal mucosa. The drugs employed were proprietary vasoconstrictors, namely, Biogan, Biogan with a preservative. Neo-Biogan, Novogan, and Cetyl-pyridinium chloride. Biogan had no deleterious effect on the mucosa of the rabbits nor did it affect the ciliary beat. The addition of a preservative did not produce any damage. Novogan and Neo-Biogan produced inflammatory changes in the mucosa, the former was less irritating than the latter. Biogan and Cetyl-pyridinium chloride 1:5,000 sprayed into the nasal cavities of rabbits three times a day for 14 days caused no demonstrable damage. However, when these drugs were continued for one month, signs of irritation appeared such as dryness, slowing of ciliary activity, and increased mucous secretion. Cetyl-pyridinium chloride 1:1,000 and 1:10,000 in isotonic saline did not produce any more irritation than the saline alone.

C.

Miscellaneous Allergies

Observations on Cold Sensitivity. Kelly, F. J., and Wise, R. A.: Am. J. Med. **15**: 431, 1953.

A 20-year-old male with a negative family and personal history for allergy developed a desquamating dermatitis of the hands while in the army. A few months later, the patient noted progressive swelling of the hands upon exposure to low temperatures. This continued even after he took up residence in a warm climate. Within 5 to 10 minutes of exposure to cold, his hands would become stiff and red, and paresthesias would be felt. Pain would ensue if the swelling became severe enough. The swelling would subside over a period of a few hours. Immersion of the hands in warm water aggravated, rather than relieved, the condition. No other part of the body was ever involved, nor were there ever any systemic symptoms. Exposure of the rest of the body to cold failed to affect the hands if they were protected. Between attacks, the skin of the hands remained normal in appearance.

The intramuscular administration of 25 mg. of ACTH 4 hours prior to exposure to cold failed to inhibit the reaction. The administration of antihistaminics also failed to inhibit the reaction. However, when 20 mg. of ACTH were given by continuous intravenous drip over a 6-hour period and there was immediate exposure to cold, no swelling occurred. Thirty to 60 minutes later, a second chilling resulted in mild swelling. Further studies revealed that the swellings were accompanied by a slight increase in pulse rate and a slight drop in blood pressure. Blood withdrawn from the antecubital vein on the side of the chilled hand was almost as red in color as arterial blood, whereas that taken from the other arm was definitely venous in color. A 30 per cent drop in the eosinophil count occurred in blood taken from the chilled side, but no change was observed in the blood drawn from the contralateral side.

After several weeks of cold applications to the hands (usually the right), the reactions in both hands began to decrease in severity. It is suggested that this is a case of localized alteration in the reactivity of the vascular tissues of the hands. It was apparently related to the original desquamating skin disease and probably associated with the liberation of H-like substances in the tissue. F.

Penicillin Reactions: Their Nature, Growing Importance, Recognition, Management and Prevention. Kern, R. A., and Wimberley, N. A. Jr.: Am. J. M. Sc. **226**: 357, 1953.

The subject of penicillin reactions has been completely reviewed. The authors noted that during the first 9 years of penicillin therapy there were only two deaths reported which could be ascribed to its use. However, in the past 18 months, fifteen deaths from penicillin were reported. They note with alarm the increasing frequency of fatal reactions and stress the fact that undoubtedly many lethal reactions which occur more insidiously, as for example from periarteritis nodosa, are not being reported as penicillin deaths. Penicillin reactions are classified into the following categories: (1) urticaria, (2) dermatitis medicamentosa, (3) erythema nodosum and multiforme, (4) contact dermatitis, (5) exfoliative dermatitis, (6) bullous dermatitis, (7) "serum sickness" reaction, (8) purpura, (9) agranulocytosis, (10) photosensitivity, (11) lupus erythematosus, (12) periarteritis nodosa, (13) anaphylaxis, (14) miscellaneous such as CNS reactions (convulsions or peripheral neuritis).

Factors which favor the development of a penicillin reaction include: (1) a previous sensitizing injection, (2) allergic (atopic) constitution, (3) parenteral injection or local application as opposed to oral administration, (4) sensitivity to other fungi, (5) combining penicillin with various adjuvants such as the depot or "Neo-Penil" form.

Circulating antibodies are demonstrable only in the severest type of penicillin reactions such as those characterized by anaphylactic responses. Before institution of penicillin therapy the authors advise that all patients with a previous history of sensitivity be scratch tested with penicillin. When the scratch test is negative an intracutaneous test with a solution of penicillin containing 5,000 units per c.c. should be done. Atopic patients with no previous history of penicillin sensitivity should be tested intracutaneously. Patients who show delayed skin reactions are likely candidates for mild reactions but rarely develop serious reactions. Although negative skin tests do not rule out the possibility of ensuing reactions the risk is much less. The authors make the following suggestions for prevention of penicillin reactions: 1. All unnecessary use of penicillin be stopped. 2. Avoid the use of depot forms of penicillin. 3. Give penicillin by mouth rather than parenterally whenever possible. 4. Do not combine penicillin with another drug when giving it parenterally. R. W.

Bone Maturation and Capillary Microscopy as Indicators for the Use of Thyroid in Childhood Allergy. Ratner, B.: Ann. Allergy **11**: 419, 1953.

Allergic children suffering from hypothyroidism may fail to respond to the usual allergic treatment. Bone maturation studies by means of roentgenographic examination of the hands and capillary microscopy offer simple and rapid methods for evaluating the status of thyroid function. In the hypothyroid state there is a retardation of epiphyseal development which is best demonstrated in children after the first year and through the prepubital period. Microscopic examination of the nail fold shows a distinctive capillary pattern in hypothyroidism which can be described as an inhibition of capillary development approximating that of the fetal stage. There is also evidence of water retention as manifested by abnormal swelling of the papillae which form transparent caps around each capillary loop. The administration of thyroid in suspected cases is begun with 0.25 or 0.5 grain per day depending on the age of the child and is increased gradually to as much as 2 grains per day until the desired effects are obtained. A markedly elevated pulse rate and signs of increased irritability are indications for reducing or discontinuing the medication. If bone maturation remains retarded in spite of therapy, thyroid can be continued for several years if the child is gaining weight and growing. The best results are obtained in eczematous patients, but good results are not uncommon in respiratory allergy. F.

Gastrointestinal Allergy and the Celiac Syndrome With Particular Reference to Allergy to Cow's Milk. Kunstadter, R. H., and Schultz, A.: Ann. Allergy, **11**: 426, 1953.

Among a group of 36 infants with diarrhea, 18 gave a history of the presence of some form of allergy in the immediate family, parents, or siblings. Fifty per cent of the cases themselves manifested frank symptoms of allergic illnesses. In 17 of the cases, the diarrhea had begun during the first 3 months of life. Eleven of the 36 patients presented the clinical picture of the celiac syndrome; 8 of these infants had a positive family history of allergy and some form of allergic disturbance before, during, or after recovery from the diarrhea. A total of 19 cases in this series required elimination of cow's milk from the diet for periods ranging from 3 to 42 months. In 8 of the 11 cases of celiac disease, cow's milk had to be eliminated for periods ranging from 11 to 42 months. Thereafter, most of these children were able to take cow's milk without recurrence of symptoms. The authors recommended that cow's milk and its products be eliminated from the diet of all children who develop troublesome diarrhea. In those cases which are due to milk sensitivity, rapid improvement usually takes place and a recurrence of symptoms follows the reintroduction of cow's milk. F.

Locust Sensitivity. Frankland, A. W.: Ann. Allergy **11**: 445, 1953.

Four of a group of 34 individuals who worked in close contact with locusts developed symptoms of allergic rhinitis and asthma. The symptoms occurred after exposure to either the locusts or their feces. Three of these patients were known to be allergic and the fourth had a positive family history for allergy. Skin tests performed with extracts made from the bodies and feces of the locust and the cockroach demonstrated a striking cross antigenicity between the two species. The author suggested the possibility that dried cockroach feces may be a component of house dust in certain instances. One patient was successfully hyposensitized with an extract of locust feces. F.

Allergic Encephalomyelitis in the Rat Induced by the Intracutaneous Injection of Central Nervous System Tissue and Adjuvants. Lipton, M. M., and Freund, J.: J. Immunol. **71**: 98, 1953.

Allergic encephalitis was induced regularly in the white rat by the intracutaneous injection of a suspension of the brain or spinal cord of the rat, guinea pig, or rabbit with the aid of adjuvants. Two factors were essential in the production of this experimental disease, namely, killed tubercle bacilli or *Nocardia asteroides* in the emulsion and the intracutaneous route of administration. Subcutaneous injections had no effect.

The manifestations of this disease in rats were flaccid paralysis of the hind legs, urinary incontinence, fecal impaction, and weight loss. Remissions occurred frequently. The most constant lesion was perivascular cuffing of mononuclear cells around venules and capillaries of the central nervous system. M. Cohen.

Reaction to PAS. Downs, W. J.: Canad. M. A. J. **69**: 67, 1953.

After having received a brief course of streptomycin therapy, a 40-year-old woman with moderately advanced tuberculosis was given PAS three times daily. Ten days later, she developed malaise, headache, and a low-grade temperature. However, these symptoms subsided quickly and she was fairly normal for the next month. At this time she again developed various complaints such as headache, abdominal pains, vomiting, chills, and fever followed by a generalized dermatitis. PAS was stopped in the next 24 hours, but the rash progressed and was accompanied by edema and vesicle formation. About 10 days later, she developed weakness, her pulse became irregular and was of poor quality. An electrocardiogram done at this time showed a slight irregularity and mild heart block with a P-R interval of .22 sec. Pyribenzamine was ineffective in relieving her symptoms and she was given BAL and sodium lactate. By the next day her temperature dropped from 103.6° to normal and her symptoms began to clear. The pulse became regular and the rash faded. It is suggested that as a part of her allergic reaction to PAS, this patient developed a myocarditis. This severe reaction responded promptly to BAL and sodium lactate. R. W.

Anaphylaxis

Quantitative Studies on Passive Cutaneous Anaphylaxis in the Guinea Pig and its Relationship to the Arthus Phenomenon. Ovary, Z., and Bier, O. G.: J. Immunol. **71**: 6, 1953.

Passive cutaneous anaphylactic reactions were induced in the guinea pig by injecting small amounts of rabbit antiserum in the skin followed in 2 to 6 hours by a mixture of antigen and dye, intravenously. A positive reaction consisted of a circular blue spot which developed at the antibody site within 15 minutes. A positive reaction could be elicited after a latent period of 30 minutes following the injection of the antibody. After 48 hours the skin became nonreactive. When circulating antibodies were removed by intracutaneously injected antigen, the intensity of passive cutaneous anaphylactic reactions was not affected. Neoantergan inhibited passive cutaneous anaphylactic reactions induced by small amounts of antibody but had little effect when large amounts of antibody were used as required for the Arthus phenomenon. Horse antibacterial typhoid serum failed to induce passive cutaneous reactions in guinea pigs but did produce severe Arthus reactions.

It is suggested that these findings point to fundamentally different mechanisms in the Arthus reaction and passive cutaneous anaphylaxis. The Arthus phenomenon seems to be due to an injurious effect on small blood vessels pro-

duced by the interaction of circulating antibody and locally injected antigen. It may be classified as a localized allergic reaction of the necrotic-hemorrhagic type. On the other hand, passive cutaneous anaphylaxis results from the interaction of fixed antibody and circulating or locally introduced antigen, leading to histamine release as in systemic anaphylaxis. M. Cohen.

Experimental Hypersensitivity. The Effect of Adrenocorticotropic Hormone, Cortisone and Adrenalectomy on the Serological and Histological Responses in the Rabbit Following Injections of Foreign Proteins. Moll, F. C., and Van Zandt Hawn, C.: J. Immunol. **70**: 441, 1953.

Rabbits were injected intravenously with large amounts of bovine-gamma-globulin and the histologic changes in the kidney, the level of serum complement, and the titers of precipitin antibodies were studied under various experimental conditions. Control animals showed a depression of the level of the serum complement, demonstrable circulating antibodies by the tenth day, and a subsiding glomerulitis at the time of sacrifice. Rabbits receiving ACTH for 12 days after immunization showed serologic patterns similar to the controls, but the histologic changes in the glomeruli were inhibited.

Cortisone inhibited antibody synthesis and the fall of serum complement levels, and also prevented the glomerulitis. Adrenalectomized animals demonstrated a regular complement drop, antibody formation, and histologic changes which were more marked than in operated nonadrenalectomized controls. It was suggested that in rabbits ACTH interfered with the production of lesions by alteration of tissue reactivity and that cortisone influenced the picture by the inhibition of antibody formation. M. Cohen.

Immunological Studies of Egg White Proteins. V. The Cross-Reaction of Egg White Proteins of Various Species. Wetter, L. R., Cohn, M., and Deutsch, H. F.: J. Immunol. **70**: 507, 1953.

By means of quantitative precipitin reactions, many proteins in the egg white of turkey, guinea hen, pheasant, duck, and goose were found to cross-react with antisera to chicken ovalbumin, conalbumin, ovomucoid, and lysozyme. Since the phenomenon of cross-reaction has been demonstrated to be due to the structural similarity of the combinants involved, a phylogenetic relationship between the various species possessing similar proteins was implied. In most of the previous studies of this problem qualitative methods were employed. M. Cohen.

Hemoglobin as a Tracer Antigen in Anaphylaxis. West, H. D., Chappelle, E. W., Clark, W. F., and Hahn, P. F.: Am. J. Path. **29**: 363, 1953.

Guinea pigs were sensitized and shocked with dog hemoglobin which had been tagged with radioactive iron. The organs of the animals were subsequently examined histologically and by radioassay. On the basis of antigen concentration, it was concluded that the lung was the primary site of anaphylaxis in the guinea pig. Radioactive hemoglobin was shown to be a valuable tool in tracer antigen studies. J. S.

Pharmacology, Physiology, and Pathology

Physiologic Studies in Atopic Dermatitis (Disseminated Neurodermatitis). 1. The Local Cutaneous Response To Intradermally Injected Acetylcholine and Epinephrine. Lobitz, W. C., Jr., and Campbell, C. J.: Arch. Dermat. & Syph. **67**: 575, 1953.

Ten patients with atopic dermatitis were injected intracutaneously with 0.1 c.c. of acetylcholine and epinephrine, in dilutions of 1:10,000 and 1:100,000.

Isotonic saline was used as a control. The areas tested included the flexor surfaces of the arms and forearms, antecubital spaces, and the skin on the back. Areas of active dermatitis and areas of normal appearing skin were tested. The white-line response was obtainable in all the tested sites following firm stroking with a sharp instrument. The responses obtained with epinephrine in these cases were essentially the same as those obtained in nonatopic individuals. Whealing did not occur, but the red flare (axon reflex) was observed in 96 per cent of the cases at the end of one minute and then gradually began to fade. Blanching (vasoconstriction) was seen in 100 per cent of the observations with pseudopod-like areas of vasoconstriction often being detected. Sweating took place in 38 per cent of the cases in one minute and in 89 per cent after 3 minutes. Comparing of the response to the intracutaneous injection of acetylcholine in atopic and nonatopic individuals revealed increased whealing in the atopic individuals, but no change in the flare or sweat response. The marked variation from the normal which occurred was the "delayed blanch" phenomenon which took place gradually and spread peripherally around the wheal.

In 20 per cent of the patients, this "delayed blanch" could be observed at the end of one minute; by the end of 15 minutes, it was present at all the test sites. The blanching remained for over 60 minutes in two patients, but usually lasted only 15 to 30 minutes. Since procaine failed to block this response, the reaction was apparently not due to an axon reflex. The authors discuss the possible mechanism of this unusual response and suggest that the "delayed blanch" from acetylcholine is the result of direct action of a vasoconstrictor substance on the blood vessels of the skin. They also present evidence supporting the probability that this substance may be acetylcholine itself.

R. W.

The In-Vitro Purification of Tissue Localizing Antibodies. Korngold, L., and Pressman, D.: J. Immunol. **71**: 1, 1953.

Antisera were obtained by injecting rabbits with various rat-tissue extracts. The tissue antibodies were labeled with radioactive iodine and then purified in vitro. The radioiodinated antibodies were absorbed with a blood vessel fraction or cellular fraction of the homologous organ and then eluted by heat. The localizing activity of each antibody was determined by intravenous injection of radioactive eluate into rats, and then analyzing the tissues for radioactivity after the animals were perfused.

The eluates from blood vessel and cellular fractions of the same organ had different localizing properties. For example, when antilung serum was purified by the cellular fraction of the lung, the eluate localized in the lung. However, when purified by the blood vesel fraction of the lung, the antibodies localized to a much greater extent in organs other than the lung. This seemed to indicate that the tissue-localizing property of an antitissue serum depended upon a mixture of antibodies each related to a corresponding antigen in the tissue. As in the case of the lung, antibodies purified by cellular fractions of liver and spleen localized in the homologous organ. For antibody localization in the kidney, however, purification with kidney blood vessel fraction was needed.

M. Cohen.

Effect of Certain Antihistaminics on Epinephrine-Induced Hyperglycemia and Lacticacidemia. Komrad, E. L., and Loew, E. R.: J. Pharmacol. & Exper. Therap. **103**: 115, 1951.

Some antihistamines increase the pressor response to epinephrine in anesthetized dogs. In the present study the effects of a variety of well-known

and experimental antihistamines were tested in rabbits and dogs to determine whether the antihistamine affected epinephrine-induced elevation of blood sugar values. The antihistamines were administered intravenously and did not affect fasting blood sugar levels. Subsequent intravenous administration of epinphrine in these test animals elicited blood sugar rises of as little as one-tenth of that observed in saline pretreated controls. The diminution in effect appeared to be related to the dose of antihistamine. In rabbits, a high degree of epinephrine antagonism was found with Histadyl, Chlorothen, Pyribenzamine, Neoantergan, and Phenergan. Less activity was observed with Chlortrimeton, Diatrin, Neohetramine, Decapryn, Perazil, Benadryl, and Thephorin. Dogs did not exhibit similar changes. In these animals, Histadyl and Chlortrimeton were found to potentiate the epinephrine hyperglycemia. Dogs could not tolerate such high dosages of these drugs as rabbits. Only Chlorothen and Thephorin reduced epinephrine hyperglycemia. The lactic acid blood levels were unaffected, suggesting "that inhibition of the effect of epinephrine on carbohydrate metabolism occurs only at the liver" and that muscle glycogenolysis was not affected by the antihistamines. Aminophylline, Nembutal, procaine, cocaine and atropine produced no effect on epinephrine hyperglycemia in rabbits. K.

Relationship Between Actions of Adrenocortical Steroids and Adrenomedullary Hormones in the Production of Eosinopenia. Henry, W. L., Jr., Oliner, L., and Ramey, E. R.: Am. J. Physiol. **174**: 455, 1953.

Small doses of cortisone (3 mg./kg.) failed to produce significant eosinopenia in adrenalectomized dogs. When epinephrine was given four hours later a significant drop in the eosinophil count occurred. Larger doses of cortisone (5 mg./kg.) produced an average fall of 61 per cent in the circulating eosinophils in adrenalectomized dogs. Epinephrine given 4 hours later did not further increase the eosinopenia. Additional studies demonstrated that epinephrine in small dosages induces eosinophilia in the adrenalectomized dog, whereas larger dosages produce eosinopenia.

Two human subjects, one bilaterally adrenalectomized and the other suffering from Addison's disease, who were being maintained on oral cortisone showed a decrease of 62 per cent in their eosinophil count after the administration of 0.3 mg. of epinephrine.

These findings suggest that there is a cooperative action between epinephrine and the C-11 oxysteroids to produce eosinopenia. F.

Effect of Continuous Injection of Epinephrine on Adrenal Cortex and Anterior Hypophysis. Coutinho, H. B., Baker, B. L., and Ingle, D. J.: Proc. Soc. Exper. Biol. & Med. **84**: 137, 1953.

Rats received massive dosages of epinephrine by continuous subcutaneous infusions for from 1 to 21 days at which time they were sacrificed. The adrenal cortex and anterior hypophysis were studied histologically for evidence of increased secretory activity. No such evidence could be found. The hypertrophy and cholesterol depletion usually induced in the adrenal cortex by repeated injections of ACTH were not present in these animals nor was the phospholipid content of the anterior hypophysis increased. These observations are in accord with recent investigations in man which also failed to demonstrate a pronounced stimulating effect of epinephrine on the hypophysis to secrete ACTH. M. Cohen.

Binding of Histamine by Animal Proteins. Kaplan, E. H., and Davis, J.: Proc. Soc. Exper. Biol. & Med. **84**: 218, 1953.

Histamine labeled with radioactive carbon was dialyzed against human γ-globulin, β,-globulin, plasma albumin, serum and guinea pig lung homog-

enate. The latter tissue was selected because of its relatively high histamine content. Tyrode solution was substituted for the proteins in the control experiments. The solutions equilibrated with protein and with Tyrode solution showed uniform distribution of histamine on both sides of the cellulose membrane. This demonstrated that labeled histamine was not bound by human blood proteins and that guinea pig lung is incapable of binding added histamine in vitro or of equilibrating added with bound histamine. It is suggested that binding of histamine requires its formation at the binding site. M. Cohen.

The Effects of Spleen Shielding and Subsequent Splenectomy Upon Antibody Formation in Rats Receiving Total-Body X-Irradiation. Wissler, R. W., Robson, M. J., Fitch, F., Nelson, W., and Jacobson, L. O.: J. Immunol. **70**: 379, 1953.

Total body x-irradiation produced a marked depression in the circulating antibody concentration of the rat in response to a single intravenous or intraperitoneal injection of foreign erythrocytes. When the spleen was exteriorized and shielded with lead during total body irradiation, the antibody-forming capacity of the animal was preserved. Under certain conditions, the route of administration of antigen appeared to be a critical factor in the production of antibodies. Antibody formation was suppressed when antigen was given intravenously 24 hours prior to splenectomy, but not when the intraperitoneal route was used. In spleen-shielded rats that were splenectomized 24 or 72 hours after irradiation, antibody formation occurred only when antigen was given intraperitoneally. The mechanism by which a shielded spleen in the irradiated rat stimulates or protects the remaining antibody forming tissue is unknown. M. Cohen.

The Occurrence of Leucocyte-Platelet Thrombosis in Rheumatic Carditis. Stetson, C. A., Jr.: J. Exper. Med. **94**: 493, 1951.

Pathologic microscopic studies were made on human beings who had died of rheumatic heart disease and on individuals who had died of other causes. Leucocyte-platelet thrombi, similar to those seen in the developing Shwartzman and Arthus lesions of rabbits, were found in the hearts of patients with active rheumatic fever and rheumatic carditis. K.

Production of Nucleophagocytosis by Rabbit Antileukocytic Serum. Zimmerman, H. J., Walsh, J. R., and Heller, P.: Blood **8**: 651, 1953.

White blood cells were obtained from the buffy coat of the peripheral bloods of patients suffering from myelocytic leukemia. The cells were allowed to dry overnight, were then ground, and suspended in saline. This suspension was injected subcutaneously into rabbits every third day for 8 weeks. Plasma obtained from these animals at 4-week intervals was tested for the "L.E." phenomenon. This procedure was carried out by mixing the rabbit plasma with cells from the antigenic source (buffy coat of leukemic patient's peripheral blood). Plasma obtained 4 weeks after sensitization produced frequent nucleophagocytosis. Many of the engulfed nuclei showed clear chromatin patterns and appeared similar to the Hargraves "tart cell." The engulfing cell was a polymorph rather than a histocyte as described by Hargraves. The "pre-L.E." cell described by Stitich (cells with varying degrees of karyorrhexis of the nuclei) also was seen. Many of the polymorphs were seen to clump together. Plasma obtained 12 weeks following sensitization revealed similar findings, but less nucleophagocytosis was observed. Specimens of plasma obtained at 16 and 20 weeks failed to show the typical findings of nucleophagocytosis. Plasma obtained from rabbits prior to sensitization as

well as normal human serum failed to produce any changes after contact with the leukemic cells. Because of the similarity between the "L. E." phenomenon and the changes produced by the antileukocytic serum, the authors suggest that the "L.E." phenomenon may be due to an antileukocytic antibody. R. W.

A Technique for Estimation of the Histaminopexic Power of Blood Serum. Laborde, C., Parrot, J. L., and Urgin, D. A.: Presse méd. **61**: 1151, 1953.

In a previous publication, the authors demonstrated that when normal human serum was added to a histamine salt solution a fraction of the histamine became inactive as determined on the isolated ileal strip of the guinea pig. They called this the "histaminopexic power" of serum. The technique of measuring the histaminopexic power is presented in detail. In over 300 estimations made in human beings, it was found that the index was zero in 94 per cent of allergic patients. An index of zero was never found in persons with a nonallergic background. I. Glazer.

Miscellaneous

Specific White Cell Lysis Produced by Combination of Rabbit Antiserum to Purified Protein (Ovalbumin, Bovine Gamma Globulin) With Homologous Antigen. The Role of Non-Precipitating Antibody. Waksman, B. H., and Gaulitz, D.: J. Immunol. **70**: 331, 1953.

Repeated subcutaneous injections of purified alum-precipitated ovalbumin or a single intraperitoneal or intravenous injection of bovine gamma globulin into rabbits produced potent sera capable of lysing white blood cells. This lytic power was found to reside in a thermostabile, nonprecipitable antibody capable of inducing passive skin sensitivity of the urticarial type in man and rabbits. The addition of homologous antigen to whole blood of sensitized rabbits resulted in a gradual increase of white blood cell lytic factor during the first 2 to 3 weeks of immunization. White blood cells of fresh normal rabbit blood were lysed in the presence of homologous antigen and sensitized serum.

No relationship was found to exist between precipitable antibody N and the specific capacity to lyse white blood cells. Fractional removal of precipitating antibody had no effect on the specific white cell lytic power of immune sera. In tests of five different sera, polymorphonuclear leukocytes were demonstrated to be the cells undergoing lysis. Lymphocytes were not affected. Nonlytic sera were capable of producing passive anaphylaxis in guinea pigs in essentially the same manner as lytic sera. The mechanism of neutrophilic leukopenia which is observed in the anaphylactic process may well be explained by the specific immunologic reaction presented in this study.

M. Cohen.

Antibody Formation in Allergic and in Normal People. Adams, D. D.: Lancet **11**: 911, 1953.

A group of 11 allergic male students suffering from either chronic asthma, hay fever, or eczema was immunized with T.A.B. vaccine (Salmonella typhi, S.paratyphi-A and S. Paratyphi-B H and O). A control group of 10 students with negative family and personal histories of allergy was similarly sensitized. Agglutination tests were done prior to sensitization, and the subjects were injected with 0.25 c.c. of the antigenic mixture. Two weeks later, the subjects were given a stimulating injection of an additional 0.5 c.c. of antigen. Agglutination tests were made on blood samples drawn at the end of the first, second, third, and fifth weeks following the initial immunizing injection. The

allergic group showed a greater antibody response which statistically was shown to be significant. It is suggested that allergic people may have an increased capacity to form antibodies. R. W.

The Reduction of the Anti-Rh Antibody Titer By Cortisone Administered During Pregnancy. Frumin, A. M., Taylor, A. G., Smith, E. M., and Dratman, M. B.: Am. J. Obst. & Gynec. **65**: 1345, 1953.

A 26-year-old woman, gravida iii, para ii, was observed in her third month of pregnancy. Her first pregnancy had been entirely normal; her second child died 4 hours after birth because of hemolytic anemia. The father was Rh positive, the mother Rh negative. The mother's anti-Rh antibody titer was found to be 1:512 in albumin and 1:64 in saline. Cortisone was administered orally in an average daily dose of 50 mg. The anti-Rh antibody titer in saline disappeared completely, while that in albumin fell as low as 1:8.

The pregnancy was uneventful and a normal spontaneous delivery occurred. The child weighed 5 pounds, 9 ounces at birth but showed definite signs of hemolytic anemia of the newborn. The infant died within 2 hours before an exchange transfusion could be completed.

The absence of abortion, kernicterus, or hydrops was encouraging in view of the high antibody titer early in pregnancy and was attributed to cortisone therapy. The failure to prevent hemolytic anemia in the infant was thought to be due to incomplete suppression of antibodies in the mother's serum. The administration of higher dosages of cortisone, early in pregnancy, in such cases is suggested. J. S.

Soyin, a Toxic Protein From Soybean III. Immunochemical Properties. Liener, I. E., and Rose, J. E.: Proc. Soc. Exper. Biol. & Med. **83**: 539, 1953.

Immunologic studies were utilized in the study of soyin, a toxic protein present in defatted soybean flour. Rabbits were immunized with highly purified soyin, and the resulting antisera were analyzed for precipitins. Several components were found in these sera, indicating the presence of minor impurities in the antigen. After correcting for impurities, the soyin content of a crude saline extract of defatted soybean flour was estimated to be approximately 10 per cent. Defatted soybean flour contained about 3 per cent soyin. There was some evidence that soyin is not absorbed when administered orally to laboratory animals. M. COHEN.

Frequency of Poliomyelitis in Patients Receiving Pollen Extract Injections. Abramson, H. A.: Ann. Allergy **11**: 435, 1953.

Among a total of 153,749 patients receiving injections of pollen extract, 29 cases of poliomyelitis were recorded. This is approximately the anticipated rate of the disease among the general population. The immunizations had no effect on the incidence of bulbar paralysis, nor did the site of injection influence the location of paralysis when it did occur. F.

The Effect of Cortisone on Local Antibody Formation. Hayes, P. S.: J. Immunol. **70**: 450, 1953.

Bacterial antigens with and without cortisone acetate were placed inside capillary glass tubing and introduced subcutaneously into the abdominal region of Swiss mice. Local agglutinins formed more slowly in the connective tissue around the open end of the glass tubing in animals with the antigen-cortisone depots than in the controls. In the former group, local phagocytic activity was reduced and the rate of bacterial escape from inside the antigen

depot was augmented. However, homologous serum and spleen agglutinins developed much earlier in cortisone-treated animals than in the controls. This effect was attributed to the phagocytosis-suppressing activity of the cortisone which allowed sufficient antigen to escape from the depot, thus stimulating the formation of systemic agglutinins. M. COHEN.

Hematoxylin Bodies Associated With Allergic Angiitis in Absence of Lupus Erythematosus. Worken, B., and Pearson, R. D.: Arch. Path. **56**: 293, 1953.

A 23-year-old Puerto Rican male began to have severe unremitting attacks of asthma about 5 months after he was inducted into the army. He was hospitalized and treated with a variety of medications, including penicillin, Aureomycin, and Chloromycetin. He showed some improvement but continued to have mild asthma which was controlled by epinephrine. A blood count on admission showed 10 per cent eosinophilia. Subsequent hemograms showed a persistent leukocytosis with a steadily rising eosinophilia, which reached 74 per cent. A sternal marrow aspiration showed a marked eosinophilia. Congestive heart failure developed and became progressively worse. Death occurred about one year after the onset of asthma.

Autopsy revealed, among other findings, intense and widespread infiltration of eosinophils in the walls of blood vessels and in the parenchyma of several organs. Aggregates of hematoxylin-staining bodies of definite morphology were found to be widely disseminated. The authors state that this is the first case reported in which hematoxylin bodies were found in a disease other than disseminated lupus erythematosis, in which they are a characteristic histologic finding. It is felt that the histologic material in this case demonstrates and confirms the previously held opinion that these bodies originate from nuclei of various cells, but predominantly from eosinophils. Allergic studies were not included in this report. J. S.

Blood Plasmacytosis in Serum Sickness. Worms, R., and Dreyfus, B.: Presse méd. **61**: 21, 1953.

One patient with a reaction to monosermicarbazone adenochrome and three patients with serum sickness were studied. All had enlarged lymph nodes. Blood studies showed leukocyte counts ranging from 10,000 to 25,000 per cmm., of which 20 to 60 per cent were plasma cells. In two patients where bloods obtained by sternal puncture were studied, there were from 8 to 17 plasma cells per 100 white blood cells. The peripheral plasmacytosis was transitory and disappeared within 6 days. This may explain why this phenomenon has not been previously reported. I. GLAZER.

Recent Aquisitions in the Treatment of Chronic Cor-Pulmonale. Celice, J., Plas, F., and Jeanson,, F.: Presse méd. **61**: 1151, 1953.

In the course of performing controlled exploratory hypertension tests by means of catheterization of the right ventricle and pulmonary arteries, an appreciable functional improvement was noted by some patients with chronic cor pulmonale. This was attributed to the heparinized serum employed in the procedure. The "Humoral Syndrome of Right Ventricular Insufficiency" comprises a polyerythemia, changes in cholinesterase, and an increased resistance test to heparin indicating hypercoagulability despite the presence of near-normal levels of prothrombin. Each of the anticoagulants, heparin, Tromexan, and sodium citrate used therapeutically produced an appreciable clinical improvement. The possible mode of action of these agents is discussed. I. GLAZER.